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Ruth Montalvo

JG-YY-4946D/500569.20085

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants: Satoru KUHARA et al.

Group: Unassigned

Serial No.: Unassigned

Examiner: Unassigned

Filing Date: January 17, 2002

Customer No.: 026418

For: DNA CHIP AND ITS PREPARATION

Commissioner for Patents  
Washington, D.C. 20231

**PRELIMINARY AMENDMENT**

Sir:

Prior to examination of the above-identified application on the merits, please amend the above-identified application as follows:

**IN THE SPECIFICATION:**

Please add the following paragraph at page 1, after the title "**DNA CHIP AND ITS PREPARATION**" on line 2 and before the heading "**FIELD OF THE INVENTION**" on line 4:

-- CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a divisional application of U.S. Application Serial No. 09/499,717 filed on February 8, 2000, which claims the priority of Japanese Patent Application No. 11-030429 filed on February 8, 1999.--

Please delete the paragraph at page 7, lines 32-34 and insert therefor the following paragraph:

--The hydrophilic polymer may be cationic, anionic, or amphoteric. A nonionic polymer is also employable. Preferred is a cationic polymer.--

Please delete the paragraph at page 16, lines 21-31 and insert therefor the following paragraph:

--The dried slide glass was scanned for detecting fluorescence strength. From the detected fluorescence strength is reduced the background fluorescence strength which was observed when a sample solution containing no fluorescence labelled-DNA fragment was spotted and treated in the same manner. Thus, processed fluorescence strength is set forth in Table 2 in terms of a relative value, in which the relative value is expressed in terms of value relative to the fluorescence strength detected on the DNA chip which was treated in the same manner except for using a solution containing no hydrophilic polymer.--

IN THE DRAWINGS:

Please delete Figures 1 and 2 and substitute therefor corrected Figures 1 and 2 which are attached hereto.

**IN THE CLAIMS:**

Please cancel Claims 1-13 and add the following new Claims 14-27.

--14. (New) A method of fixing an oligonucleotide or a polynucleotide to a solid carrier which comprises the step of spotting an aqueous solution containing the oligonucleotide or the polynucleotide and a hydrophilic polymer onto the solid carrier.--

--15. (New) The method of Claim 14, wherein the oligonucleotide or the polynucleotide is fixed to the solid carrier at its one end portion.--

--16. (New) The method of Claim 14, which further comprises the steps of washing the carrier resulting from the spotting step and drying the carrier resulting from the washing step.--

--17. (New) The method of Claim 14, wherein the solid carrier is selected from the group consisting of a glass sheet, a silicon sheet and a polymer sheet.--

--18. (New) The method of Claim 14, wherein the solid carrier is a glass sheet.--

--19. (New) The method of Claim 18, wherein the glass sheet is pre-treated with poly-L-lysine, polyethylene imine or polyalkylamine.--

--20. (New) The method of Claim 18, wherein the glass sheet is pre-treated with a silane coupling agent having an amino group, an aldehyde group or an epoxy group.--

--21. (New) The method of Claim 14, wherein the oligonucleotide or the polynucleotide has a functional group selected from the group consisting of an amino group, an aldehyde group, a thiol group and a biotin group.--

--22. (New) The method of Claim 14, wherein the hydrophilic polymer is a nonionic polymer or a cationic polymer.--

--23. (New) The method of Claim 14, wherein the hydrophilic polymer is a cellulose derivative.--

--24. (New) The method of Claim 14, wherein the hydrophilic polymer is selected from the group consisting of polyacrylamide, polyethylene glycol, polyvinyl alcohol and saccharide.--

--25. (New) The method of Claim 14, wherein the aqueous solution contains the hydrophilic polymer in an amount of 0.1 to 2.0 vol.%.--

--26. (New) The method of Claim 14, wherein the carrier resulting from the spotting step is heated.--

--27. (New) The method of Claim 14, wherein the carrier resulting from the spotting step is exposed to UV irradiation.--

## **REMARKS**

As a result of the foregoing amendment, Claims 1-13 have been cancelled and Claims 14-27 have been added. Accordingly, Claims 14-27 are pending in this application.

This application is a divisional application of U.S. Application Serial No. 09/499,717 filed on February 8, 2000 and is directed to the subject matter in non-elected Claims 10-12 in parent U.S. Application Serial No. 09/499,717. Accordingly, Applicants have hereinabove amended the specification to include a cross-reference to related applications. A copy of page 1 with the changes made herein shown in red ink is enclosed herewith.

In addition, Applicants have hereinabove amended page 7 to correct a spelling error and page 16 to correct an informal error which the Examiner of the parent case objected to. A copy of the paragraphs amended on pages 7 and 16 as they originally existed with the changes made herein shown with brackets and underlines is enclosed herewith. No new matter has been added in the specification.

Applicants have also hereinabove amended the drawings to delete Figures 1 and 2 and substitute therefor corrected Figures 1 and 2. Applicants have corrected Figures 1 and 2 to make the lines, numbers and letters uniformly thick and well defined. A marked-up copy of original Figures 1 and 2 showing the changes made in black ink is enclosed. No new matter has been added in the drawings.

Applicants have also hereinabove amended the claims to cancel Claims 1-13 and add Claims 14-27. Claims 14-16 are essentially the same as cancelled Claims 10-12. Support for Claims 17-20 is found in the specification at page 6, lines 20-36. Support for Claims 21 and 22 is found in the specification at page 7, lines 10-14 and 32-33. Support for Claims 23 and 24 is found in the specification at page 8, lines 11-17. Support for Claims 25-27 is found in the specification at page 9, lines 7-8, 28-30 and 32-34. No new matter has been added in new Claims 14-27.

In view of the foregoing, it is submitted that this application is now in condition for examination on the merits and prompt notice of allowance is earnestly solicited.

Respectfully submitted,

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January 17, 2002

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JEG/SRP

**MARKED-UP COPY OF PARAGRAPHS AMENDED IN THE SPECIFICATION**

**PARAGRAPH AT PAGE 7, LINES 32-34**

The hydrophilic polymer may be cationic, anionic, or amphoteric. A [nonionic] nonionic polymer is also employable. Preferred is a cationic polymer.

**PARAGRAPH AT PAGE 16, LINES 21-31**

The dried slide glass was scanned for detecting fluorescence strength. From the detected fluorescence strength is reduced the background fluorescence strength which was observed when a sample solution containing no fluorescence labelled-DNA fragment was spotted and treated in the same manner. Thus, processed fluorescence strength is set forth in Table 2 in terms of a relative value, in which the relative value is expressed in terms of value relative to the fluorescence strength detected on the DNA chip which was treated in the same manner except for using a solution containing no hydrophilic polymer.

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a divisional application of U.S. Application Serial No. 09/499,717 filed on February 8, 2000, which claims the priority of Japanese Patent Application<sup>1</sup>- No. 11-030429 filed on February 8, 1999.

DNA CHIP AND ITS PREPARATION

FIELD OF THE INVENTION

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This invention relates to a DNA chip favorably employable for detecting a DNA fragment complementary to oligonucleotide or polynucleotide attached to the DNA chip and its preparation.

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BACKGROUND OF THE INVENTION

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In the gene analysis in the fields of biochemistry and clinical test, the detection of a DNA fragment having a specific base sequence is performed by way of a hybridization method, particularly Southern hybridization method (i.e., Southern blotting method). Southern hybridization is performed by the steps of cleaving a DNA to be examined (i.e., sample DNA) by the use of a restriction enzyme to give its fragments; separating the DNA fragments having different molecular sizes by electrophoresis on agarose gel or polyacrylamide gel; subjecting the separated DNA fragment to treatment for giving a single stranded DNA fragment; fixing the single stranded DNA fragment onto a polyamide filter or a nitrocellulose filter; hybridizing the fixed single stranded DNA with a probe DNA (i.e., a single stranded DNA which is complementary to the fixed single stranded DNA and which is labelled with RI (i.e., radioactive isotope); washing the filter; and subjecting the filter to autoradiography for visualizing the hybridized DNA fragment on the filter.

The conventional methods using radioisotope label such as Southern hybridization method have a disadvantageous feature that they need radioisotopes which should be treated with extremely high care. Moreover, the autoradiographic process requires a long period of time such



# FIG. 1

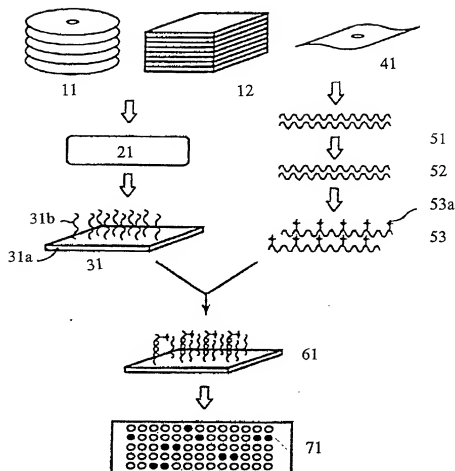
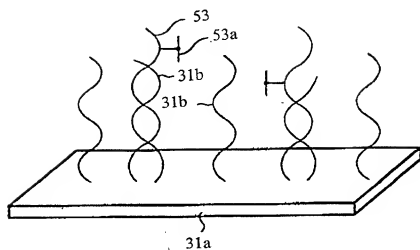


FIG.2



MARKED-UP COPY OF ~~THE~~ FIGURES 1 AND 2

FIG.1

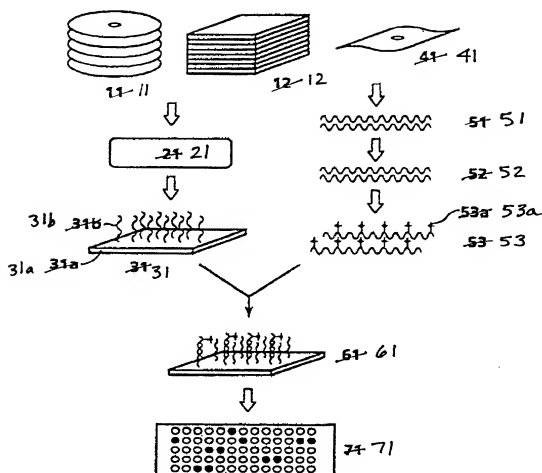


FIG.2

